

INTERNATIONAL SEARCH REPORT

Rec'd PTO

26 MAY 2005

Int'l Application No.
EP 03/13469

10/536782

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/185 A61K9/28 A61P3/10 A61P7/00 A61P9/00
A61P13/12 A61P15/10 A61P27/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, WPI Data, PAJ, EMBASE, MEDLINE, SCISEARCH, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>RUIZ E ET AL: "Effects of calcium dobesilate on the synthesis of endothelium-dependent relaxing factors in rabbit isolated aorta"</p> <p>BRITISH JOURNAL OF PHARMACOLOGY, vol. 121, no. 4, 1997, pages 711-716, XP001189345</p> <p>ISSN: 0007-1188</p> <p>cited in the application abstract</p> <p>page 715, column 1, paragraph 1 - paragraph 2</p> <p>page 715, column 2, paragraphs 1-4</p> <p>---</p> <p>-/--</p>	1-3, 6-9, 12-14

☒

Further documents are listed in the continuation of box C.

☒

Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

19 April 2004

Date of mailing of the international search report

29/04/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Cielen, E

INTERNATIONAL SEARCH REPORT

Inte al Application No

CT/EP 03/13469

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97/37647 A (ESTEVE SOLER JOSE ;ESTEVE LABOR DR (ES)) 16 October 1997 (1997-10-16) cited in the application	1-8,10, 12-15,25
Y	the whole document	16-24
X	REUTER H: "Calcium dobesilate" ZEITSCHRIFT FUR ALLGEMEINMEDIZIN 1975, vol. 51, no. 6, 1975, pages 292-293, XP008029802 the whole document	1-3,6-9, 13-15
X	ADANK C ET AL: "Calcium dobesilate in diabetic retinopathy. A retrospective controlled study." OPHTHALMOLOGICA. JOURNAL INTERNATIONAL D'OPHTALMOLOGIE. INTERNATIONAL JOURNAL OF OPHTHALMOLOGY. ZEITSCHRIFT FUR AUGENHEILKUNDE, (1985) 190 (2) 102-11. , XP008029583 abstract table I page 105, column 1, paragraph 3 page 108, column 2, paragraph 2 - paragraph 3 page 110, column 1, paragraph 1	1-3,6-9, 14,15
X	KEDZIORA-KORNATOWSKA K ET AL: "The effect of calcium dobesilate on lipid peroxidation and antioxidative defense in diabetic kidney" NEPHROLOGY DIALYSIS TRANSPLANTATION, vol. 16, no. 6, June 2001 (2001-06), page A78 XP008029588 Annual Congress of the European Renal Association and the European Dialysis and Transplant Associati;Vienna, Austria; June 24-27, 2001 ISSN: 0931-0509 the whole document	1-3,6,7, 11,14
X	TEJERINA T ET AL: "Calcium dobesilate: Pharmacology and future approaches" GENERAL PHARMACOLOGY, vol. 31, no. 3, September 1998 (1998-09), pages 357-360, XP002233076 ISSN: 0306-3623 abstract page 357, column 1, paragraph 3 page 357, column 2, paragraph 1 - paragraph 2	1-3,6-9, 12-15

-/--

INTERNATIONAL SEARCH REPORT

International Application No

T/EP 03/13469

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>GUERRINI M ET AL: "Calcium dobesilate in the treatment of diabetic microangiopathy: a chronic controlled open study on the hemorheological and microcirculatory changes"</p> <p>RIFORMA MEDICA 1988 ITALY, vol. 103, no. 1-2, 1988, pages 7-12, XP008029582</p> <p>ISSN: 0035-5259</p> <p>abstract</p> <p>page 8, column 1, paragraph 4</p> <p>page 11, column 2, paragraph 2</p>	1-3,6-9, 11,13-15
X	<p>DATABASE EMBASE 'Online!'</p> <p>ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL; 1973</p> <p>TEMPRANO ACEDO J: "Clinical trials of calcium dobesilate in diabetic retinopathy"</p> <p>Database accession no. EMB-1974137352</p> <p>XP002276559</p> <p>abstract</p> <p>& ANALES DEL INSTITUTO BARRAQUER 1973, vol. 11, no. 1-2, 1973, pages 9-16,</p>	1-9,14, 15
Y	<p>FR 2 656 525 A (DELALANDE SA)</p> <p>5 July 1991 (1991-07-05)</p> <p>page 2, line 23 - line 32</p> <p>page 4, line 21 - line 25</p> <p>example 3</p> <p>claim 1</p>	16-19,22
Y	<p>DE 100 16 356 A (BEISEL GUENTHER)</p> <p>4 October 2001 (2001-10-04)</p> <p>column 1, paragraph 1 - paragraph 2</p> <p>column 2, paragraph 12</p> <p>column 3, paragraphs 17,19,20</p> <p>column 4, paragraphs 26,27</p> <p>column 7, paragraph 63</p> <p>column 8, paragraph 87</p> <p>column 9, paragraphs 95,96</p> <p>claims 1-4,8</p>	17-24

-/--

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/EP 03/13469

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	ANGULO JAVIER ET AL: "Calcium dobesilate potentiates endothelium-derived hyperpolarizing factor-mediated relaxation of human penile resistance arteries." BRITISH JOURNAL OF PHARMACOLOGY, vol. 139, no. 4, June 2003 (2003-06), pages 854-862, XP001189343 ISSN: 0007-1188 (ISSN print) abstract page 855, column 2, paragraph 2 page 860, column 1, paragraph 3 page 860, column 2, paragraph 2 - paragraph 3	1-3,6-8, 10,14
T	ANGULO JAVIER ET AL: "Diabetes impairs endothelium-dependent relaxation of human penile vascular tissues mediated by NO and EDHF." BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 312, no. 4, 26 December 2003 (2003-12-26), pages 1202-1208, XP004476405 ISSN: 0006-291X abstract page 1203, column 1, paragraph 2 figure 6 page 1205, column 1, paragraph 1 -page 1206, column 1, paragraph 2 page 1206, column 2, paragraph 3	1-3,6,7, 10

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-7 and 14-25 relate to the treatment of diseases which actually are not well defined. The use of the definitions "for the regulation of nitric oxide (NO) synthesis and/or the regulation of EDHF (Endothelium-Derived-Hyperpolarizing-Factor) in the endothelium of diabetic patients" and "for the prophylaxis and/or treatment of disorders based on an impairment of nitric oxide production and/or impairment of regulation of EDHF function" in the present context is considered to lead to a lack of clarity within the meaning of Article 6 PCT. It is not fully possible to determine the diseases for which protection might legitimately be sought. The lack of clarity is such as to render a meaningful complete search impossible. Consequently, the search has been restricted to the real and defined diseases mentioned in claims 8-13.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

national application No.
PCT/EP 03/13469

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. Application No
/EP 03/13469

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9737647	A	16-10-1997	FR 2747040 A1	10-10-1997
			WO 9737647 A1	16-10-1997
			AU 715600 B2	03-02-2000
			AU 2693697 A	29-10-1997
			BR 9708595 A	03-08-1999
			EP 0954298 A1	10-11-1999
			JP 2000508308 T	04-07-2000
			NO 984572 A	30-09-1998
			US 6147112 A	14-11-2000
			US 6403643 B1	11-06-2002
			CA 2251226 A1	16-10-1997
			ES 2127132 A1	01-04-1999
FR 2656525	A	05-07-1991	FR 2656525 A1	05-07-1991
DE 10016356	A	04-10-2001	DE 10016356 A1	04-10-2001
			DE 20023135 U1	03-04-2003

THIS PAGE BLANK (ASPTO)